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Genomic drivers of human cancers: Diagnostics, prognostics and therapeutics

Accurate prediction of clinical courses of human cancers remains elusive. In recent studies, we performed whole genome analysis on prostate and liver cancers. Our result showed that combination of genome copy number variance and novel fusion transcripts specific for cancer achieved high accuracy in predicting clinical outcomes of these cancers. Interestingly, some of these fusion genes are also present in a variety of human malignancies. Some of these fusion gene products trigger new pathways that are essential for carcinogenesis in multiple human cancers, and create novel functions that are not present in wild type gene counterparts. Treatment of cancers with drugs specific for fusion genes and their signaling pathways produced dramatic improvement of metastasis and survival rate of animals xenografted with cancers positive for these fusion genes. Our analyses suggest that targeting therapy for fusion genes holds promise as an effective treatment for human cancers.

Biography

Jianhua Luo has been studying Molecular Pathology related to human malignancies in the last 24 years. Currently, he is a Professor of Pathology and Director of High Throughput Genome Center at University of Pittsburgh. In the last 16 years, he has been largely focusing on "Genetic and molecular mechanism of human prostate cancer and hepatocellular carcinomas". In this period, his group has identified and characterized several genes that are related to prostate cancer and hepatocellular carcinoma, including SAPC, myopodin, CSR1, GPx3, ITGA7, MCM7, MT1h and GPC3. He has characterized several signaling pathways that play critical role in prostate cancer development, including myopodin-ILK-MCM7 inhibitory signaling, myopodin-zyxin motility inhibition pathway, CSR1-CPSF3, CSR1-SF3A3 and CSR1-XIAP apoptotic pathways, MT1h-EHMT1 epigenomic signaling, ITGA7-HtrA2 tumor suppression pathway, GPx3-PIG3 cell death pathway, AR-MCM7 and MCM7-SF3B3 oncogenic pathways. He proposed prostate cancer field effect in 2002. He is one of the pioneers in utilizing high throughput gene expression and genome analyses to analyze field effects in prostate cancer and liver cancer. He is also the first in using methylation array and whole genome methylation sequencing to analyze prostate cancer. Recently, his group found that patterns of copy number variants of certain specific genome loci are predictive of prostate cancer clinical outcomes, regardless tissue origin. His discovery of several novel fusion transcripts and their association with aggressive prostate cancer has brought significant new insight into the field of prostate cancer research. Overall, these findings advance our understanding on how cancer develops and behave, and lay down the foundation for better future diagnosis and treatment of human malignancies.

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